Congressman Roscoe Bartlett
Congressional Record
House of Representatives
June 7, 2005
STEM CELL RESEARCH
Pages: H4179-H4184
GPO's PDF
@10:15 p.m.

The SPEAKER pro tempore. Under the Speaker's announced policy of January 4, 2005, the gentleman from Maryland (Mr. *Bartlett*) is recognized for 60 minutes.

Mr. BARTLETT of Maryland. Mr. Speaker, a couple of weeks ago on this floor there was a very prolonged and serious debate on stem cells. Now that we have had time for emotions to subside, I thought it might be productive to spend a little while this evening talking about the subject of stem cells and why there is so much interest in it across the country.

A few months ago there was so much interest in this subject in California, for instance, that the voters voted favorably for a resolution that would make $3 billion from California taxpayers available to do research on embryonic stem cells.

What are stem cells? We have a chart here which kind of shows this.

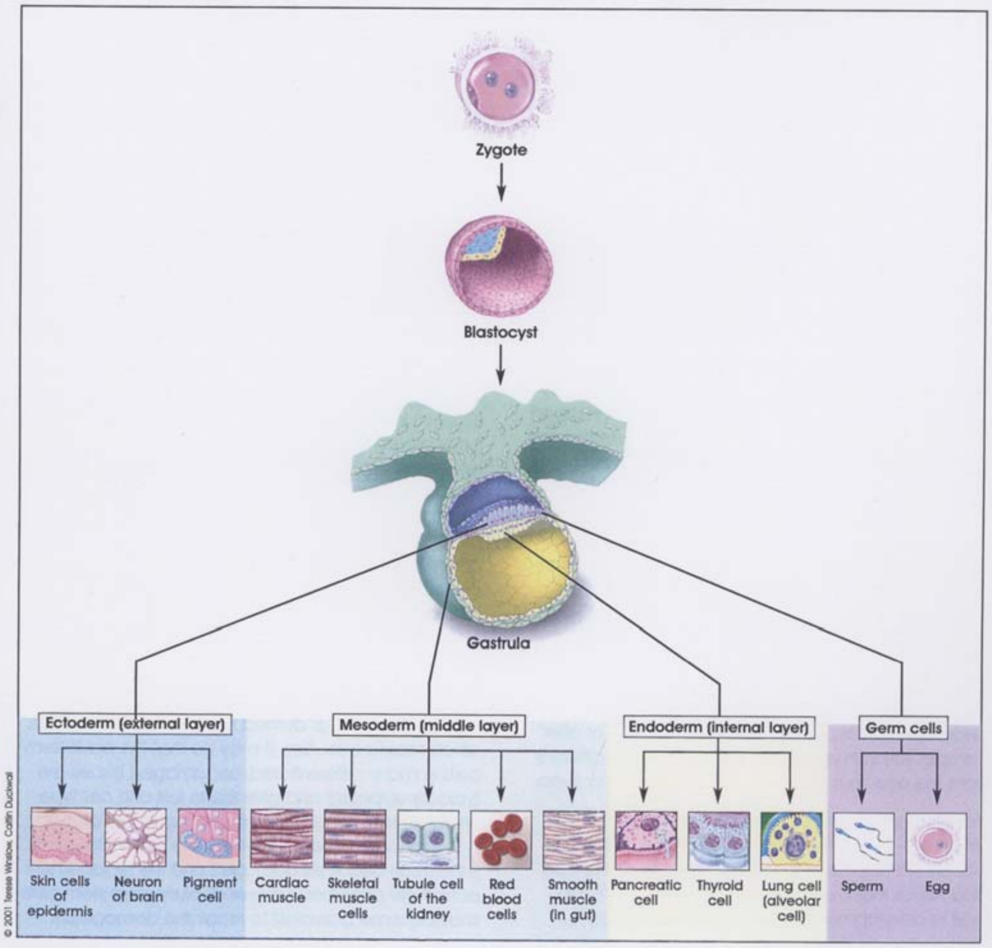

Figure 1.1. Differentiation of Human Tissues.

tissue; it can renew itself and become specialized to yield all of the specialized cell types of the tissue from which it originated. Adult stem cells are capable of self-renewal for the lifetime of the organism. Sources of adult stem cells have been found in the bone marrow, blood stream, cornea and retina of the eye, the dental pulp of the tooth, liver, skin, gastrointestinal tract, and pancreas. Unlike embryonic stem cells, at this point in time, there are no isolated adult stem cells that are capable of forming all cells of the body. That is, there is no evidence, at this time, of an adult stem cell that is pluripotent.

[Time: 22:15]

There are fundamentally two types of stem cells. There are adult stem cells and there are embryonic stem cells.

I guess the ultimate stem cell is the fertilized ovum, which is referred to here as a zygote, because from that cell develops all the cells of the body. That single cell, produced from the union of the egg and the sperm, divides and divides again and again until finally it is a blastocyst; and then it goes to the gastrula stage, and at that stage the three germ layers begin to sort out the cells that are already differentiating, is the technical term that is used for that.

Every cell in our body, of course, has all of the same gene complement. And by mechanisms that are not clearly understood, during the embryonic process genes get turned on and get turned off, and the cells that are destined to produce your skin, for instance, the genes that are producing all the other tissues of the body are turned off, and only those genes necessary for producing the skin are still active.

Here we have the three germ layers: The ectoderm, which is the outer layer, and from that will develop your skin and your nervous system.

Then we have the mesoderm, that will be the middle layer, meso meaning middle, and from that will develop most of the weight of your body, all of your skeletal muscle, your cardiac muscle, much of the kidney, the blood cells, the smooth muscle in your intestines and stomach and so forth.

Then from the innermost layer of this inner cell mass as it is called here, the mass of cells that differentiates into these three germ layers, the endoderm, the internal layer, produces not very much of the mass of your body, the pancreatic cell and the thyroid gland and the lining of the things like your lung and intestines and so forth are produced from the endoderm.

Then, of course, there are the unique germ cells produced, the sperm in the male and the egg or the ova in the female.

The reason for the intense interest in these stem cells is because of the perceived potential for affecting the course of many diseases and hopefully curing many of our diseases.

We have fundamentally two kinds of problems with our health. One is from tissue deficiencies when the tissue no longer does the kind of thing that it was destined to do and this embryonic development is wearing out or diseased. Then we have diseases from pathogens. These are organisms that can be outside that invade us.

Primarily, the hope is that stem cells will be useful in treating diseases of tissue deficiency. Although if the pathogens have destroyed a tissue and then the body has marshaled its resources with the help of the doctors with the antibiotics and so forth so that the pathogen is destroyed, then there is some hope that through the use of stem cells that you might be able to repair or replace the tissue damaged by the pathogen.

There are a lot of examples of diseases that might be amenable to cure or at least assistance through these stem cells. One is diabetes, which is a deficiency of insulin. Insulin is produced by some little cells that look like islands under the microscope because they are very dissimilar to the cells that they find themselves in. These cells are distributed through the tissue of the pancreas.

The pancreas is a big gland that produces a lot of enzymes. When the food leaves the stomach and goes into the small intestine, the pancreas produces enzymes for the digestion of fats, carbohydrates and proteins. So it is a very important digestive gland.

There is no real reason why these little islands of tissues, called the islets of Langerhans, named for the person who first described them, need to be in the pancreas, but that is where they are. They could, in fact, be any part of your body and do the same thing, which is secreting insulin.

We use insulin to treat persons with diabetes, but everyone knows, particularly the family of those and the patients who have diabetes, that insulin does not cure the disease. It simply prolongs life, but, ultimately, even with insulin, many of the people who have diabetes will end up having peripheral vascular problems with maybe amputation of toes or limbs, usually the lower limb, have problems in the eyes with the peripheral vascular tissue and have vision problems.

Diabetes is the most expensive disease that we have. It costs more to maintain and treat the people with diabetes than any other disease. There is the hope that if we could generate islets of Langerhans cells from these stem cells that you could eradicate diabetes, that you could implant these cells in the body, and it could be in any tissue. It could be in muscle tissue or under the skin. You could implant these islets of Langerhans cells there that produce insulin and whatever else these cells do that is not done simply by replacing the insulin which is lost. We might be able to eradicate diabetes, which, of course, would be an enormous contribution.

This is one of the most heart-wrenching things that the congressmen see, is when these little kids come to your office, they have to prick their finger maybe a dozen times a day, and they need insulin so frequently that they have an embedded little pump under their skin, about the size of a hockey puck. They may have to wake up during the night and prick their finger so that they can set the pump so it produces the right amount of insulin.

This is just one of many diseases that authorities in medicine and the general public believe might be helped with stem cell research: multiple sclerosis, lateral sclerosis, Lou Gehrig's disease.

That is one that I am personally very familiar with. My grandmother died from that disease. This was a long time ago, and it took quite a long time to diagnose that disease. She was falling. For quite a while they did not know why, and finally they diagnosed it as Lou Gehrig's disease, as was the common name for it then. I remember watching my grandmother deteriorate until the only motion that she had left, that she could communicate with us, was blinking her eyes: once for yes and two for no. Then she slowly died when she could no longer eat or drink. She did not want to be force-fed.

We did not have any dream then of stem cells and what they might do for that disease, but I can understand the hope that families have who have a loved one who has a disease like this and the hope that they have that there may be a medical advance and a miracle cure for the disease.

Alzheimer's disease, my mother had Alzheimer's disease. How nice it would have been to have turned back the clock in her mind so that she was the mother that I spent the first 60 years with.

Then, of course, there is a very large category of autoimmune diseases. I have a list here of 63 autoimmune diseases. That is an interesting type of disease. When we are developing in our mother's womb very early and our heart is beating and we have a circulatory system and we have white cells, there is a particular kind of white cell called the T cell. Very early in our embryonic development those T cells are imprinted with who we are, and that is very necessary because they have to understand who we are, who you are, who I am, so that if some foreign invader comes in there or virus or bacterium or something, they recognize that as being foreign so that they can reject it.

For reasons that we do not understand, occasionally our autoimmune mechanisms get confused, and they see some of us as not being us, as being foreign, and so they attack it. We call those autoimmune diseases, and there are a lot of those autoimmune diseases: Addison's disease, autoimmune hemolytic anemia, autoimmune hepatitis. It goes on for 63 of these diseases.

Multiple sclerosis is one of those, by the way. Lupus was one of the first of these diseases that was identified as an autoimmune disease. There is a hope that stem cells could be useful in treating all of these diseases.

Then, of course, there are the injuries of central nervous tissue. We have two kinds of nervous tissue in our body, the central nervous tissue that is in our brain and spinal cord and then the peripheral nerves. That is the nerves that run to and from the brain and spinal cord. For reasons that are difficult to understand, they have two very different responses to injury.

Peripheral nerves regrow very easily. There is a classic phenomenon known as Wallerian degeneration and then regeneration of the nerve. If you cut a nerve well in your leg that goes to your toe, it may be a long while before you get feeling back to your toe, almost always, unless a lot of scar tissue develops where the nerve was cut.

But for some reason that we do not yet understand central nervous tissue has no power to regenerate. Of course, what we are trying to do medically is to find out why central nervous tissue is different than peripheral nervous tissue, but absent finding out why so that you can turn that around there is the hope that with these stem cells we could grow nerve tissue that could then be placed in the body, injected in the body to help repair.

So there are a lot of diseases out there that medical specialists and the public generally believe could be cured or at least the course of the disease quite favorably changed with the use of stem cell technology.

There are, of course, two kinds of stem cells: embryonic stem cells and adult stem cells. Most of the work that we have done so far is with adult stem cells because we have been working with them for over three decades. We have been working with embryonic stem cells just a little over 6 years, and so the techniques for using adult stem cells are far better developed.

So there are more medical applications from adult stem cells than there are from embryonic stem cells, but we have not had enough time working with embryonic stem cells to determine whether or not they have the increased potential that most people believe they should have. The medical specialists believe this. The general public understands this.

If you are dealing with a cell that is not differentiated, that is, that it has not developed far enough along so that genes are turned off, a lot of leads are turned off, it could then develop into anything and everything with proper manipulation in the laboratory. So that if you are using embryonic stem cells there is the hope that they should have a wider application than adult stem cells.

[Time: 22:30]

There is another interesting characteristic of embryonic stem cells, and I do not know how important it will be. Only research will determine that.

At least 50 years ago, embryologists had determined that you could take a mother white mouse and a mother black mouse, each of which was pregnant and they have multiple babies in their uterus, and you could go into the uterus of the black mouse and take a little patch of skin out of the black mice, you could sew it into the skin of one of the white mice. When the white mouse is born, it has a little patch of black skin. Quite amazingly, it is not rejected.

Everybody knows when you transplant an organ from one person to another, there is a big rejection reaction to that. So we have a lot of anti-rejection drugs that we give. The person who gets that organ transplant must take those anti-rejection drugs. As soon as they stop taking them, the T-cells recognize this thing as foreign and start to attack it. Its use in the body is destroyed.

I do not know whether this little mouse experiment, whether the miracle of no rejection is a donor phenomenon or host phenomenon; but when you take skin from one embryo to another, there is no rejection. So using embryo stem cells, they might be less rejected. That would be good news.

I would like to spend just a couple of moments reflecting on some of the elements of a debate here in this Chamber. These debates are a bit like a battle. They are a battle; you are fighting for your position. Like all battles, emotions rise and sometimes things are exaggerated a little by one side or another. Now that emotions have subsided and we are dealing with other issues, I thought it might be instructive to look at some of the arguments made on both sides.

The argument on the pro-life side was that life is sacred, that these little embryos are human life, and the President has a position which I very strongly support, that it is just morally wrong to take one life hoping you can help another life. There has got to be another way to do it.

The bill we were debating said we should take some of those 400,000 surplus embryos that were produced in the in vitro fertilization clinics that were going to be discarded anyhow, we should take those embryos and use them to produce embryonic stem cell lines. For the last 4 years we have been dealing with what started out as maybe 60 cell lines, which has now dwindled down to 22, all of them contaminated with mouse feeder cells so they are only good for research. They would not be good for medical use so there is a need for additional embryo stem cell lines. These are the only stem cell lines we can use Federal money exploring. The private sector can destroy all of the embryos they wish; there is no prohibition. You just cannot use Federal money so there are only 22 cell lines we can use Federal money to explore.

The argument on the pro-life side, and I subscribe to that argument, that for any one embryo, there is no certainty that embryo is going to be destroyed, that it is going to be abandoned. The argument on the other side is there are 400,000 of them. Of course they are, you cannot keep them frozen forever, and by and by they will be discarded. But not all of them, because we now have, I understand, over 100 babies who have been born from adoption of these snowflake embryos.

We have surplus embryos because when you go for in vitro fertilization, under hormone stimulation the mother produces more than one ovum; and they are put in a petri dish and exposed to sperm and fertilized. Then the doctor watches their growth, and the doctor chooses generally several because they do not all adhere to the uterus and grow to become babies, and so he wants to be sure there will be at least a baby. So he implants several in the uterus, and there are several left over that are then frozen in the event none of those take or the mother wants to have a baby later.

I remember when I was running a farm several years ago, I was breeding cattle to a bull that had been dead for 8 years. I do not know how long the sperm and the ovum or these embryos will survive frozen, but they will survive for quite a long time.

The argument on the pro-life side is that for any one of those embryos, it could be adopted; and that is true. If you have a reverence for life, as I do, you need to find another way to pursue embryonic stem cell research without destroying embryos, and we have a bill that does just that. We have talked to experts from NIH and others around the country, and in a few moments I will be talking about that bill.

One of the arguments made by the pro-life people is we have had 58 medical applications from adult stem cells and none from embryonic stem cells, and that is true. But as Paul Harvey would say, the rest of the story is maybe the reason it is true is because we have spent 3 decades working with adult stem cells and only about 6 years working with embryonic stem cells, and you will not know if they have the same potential until you have an equivalent amount of time to work with them.

The arguments on the other side were that these cells are going to be thrown away anyhow and why not get some use from them. I have just reiterated my argument, which is the argument of the pro-life community, which is for any one of those embryos they could be adopted. In fact, some of these snowflake babies came to the White House during this debate, so they can be adopted.

There was another bill that we voted on that night and that was the umbilical cord blood bill which many mothers are now having frozen because there are some stem cell-like cells there that might be useful. But the argument is although they might be useful, they would not be as useful as the embryonic stem cells themselves.

``As a physician-scientist,'' and this is a direct quote from Curt Civin, co-director, Division of Immunology and Hematopoiesis Sydney Kimmel Comprehensive Cancer Center, one of the centers at John Hopkins University School of Medicine, and we are fortunate in our State to have one of the best universities and one of the best medical schools in the world, that is Johns Hopkins, he says, ``As a physician-scientist who has done research involving umbilical blood cord stem cells for over 20 years, I am frequently surprised by the thought from nonscientists that cord blood stem cells may provide an alternative to embryonic stem cells for research. This is simply wrong,'' he says.

By the way, all of the 58 diseases that have had applications from adult stem cells, all of them are represented by organizations that support embryonic stem cell research because the general belief is there ought to be more potential from embryonic stem cells than from adult stem cells.

Just a little history why I am standing here this evening and how I got involved in this. I did not come to this Congress until, and this was 13 years ago, until I was 66 years old, and so I had a former life. In that former life, I was a scientist. I have a Ph.D. in human physiology. I taught medical school and postgraduate medicine and spent a number of years doing research at medical schools and at the National Institutes of Health.

Several years ago, in 2001, I believe it was, there was a little like symposium at the National Institutes of Health where staff and members went out. I went out with a fairly large number of staff members where the experts from NIH were briefing the staff and members who were there on stem cell research. This was just before the President came down with his executive order on stem cells, and this was kind of an educational activity on the part of NIH. There were several researchers there; and as we can see in the next chart, I suggested it ought to be possible to take cells from an early embryo without hurting the embryo and that was because of my knowledge of what happens in twinning.

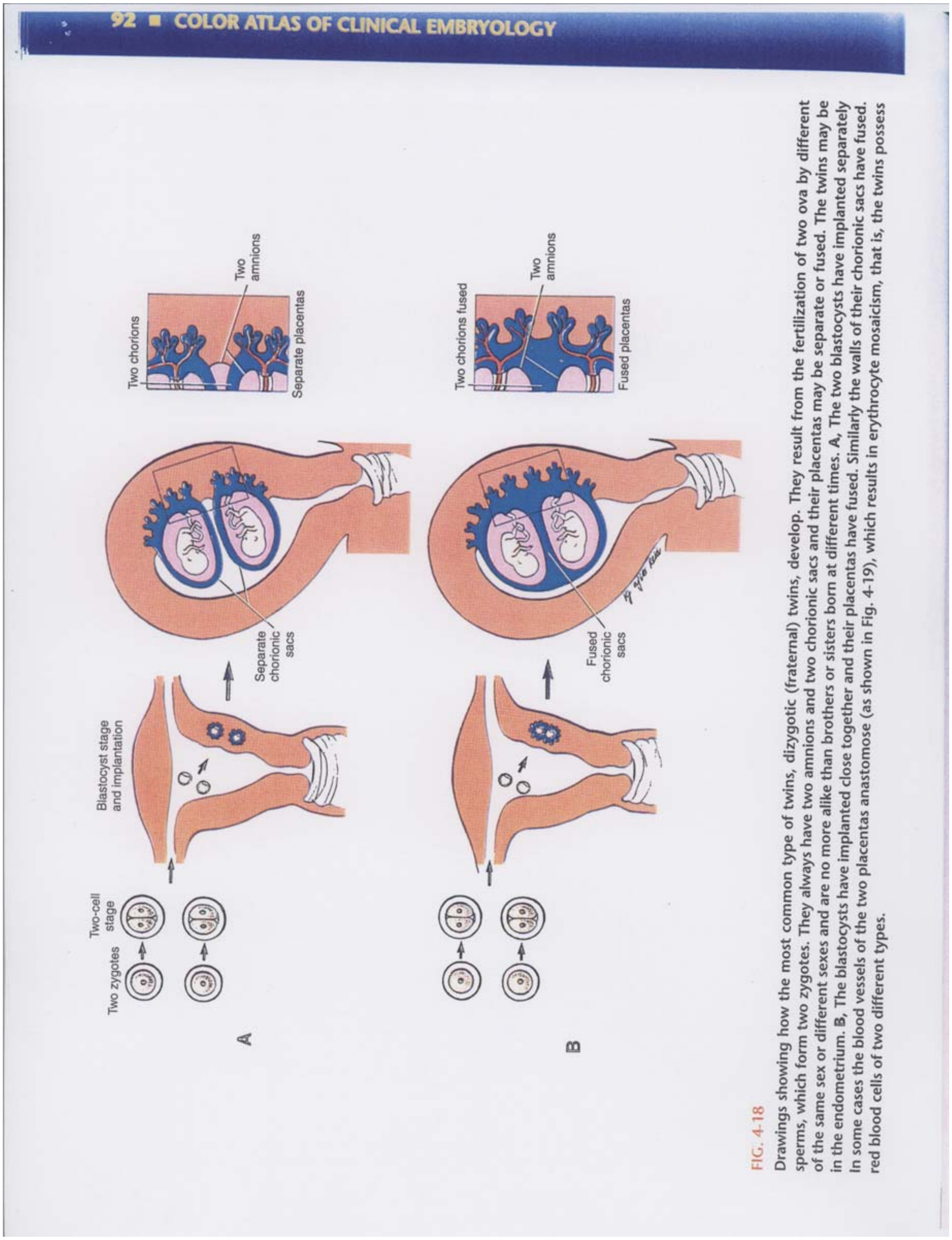

FIG. 4-18

Drawings showing how the most common type of twins, dizygotic (fraternal) twins, develop. They result from the fertilization of two ova by different sperms, which form two zygotes. They always have two amnions and two chorionic sacs and their placentas may be separate or fused. The twins may be of the same sex or different sexes and are no more alike than brothers or sisters born at different times. **A**, The two blastocysts have implanted separately in the endometrium. **B**, The blastocysts have implanted close together and their placentas have fused. Similarly the walls of their chorionic sacs have fused. In some cases the blood vessels of the two placentas anastomose (as shown in Fig. 4-19), which results in erythrocyte mosaicism, that is, the twins possess red blood cells of two different types.

Now, the first chart here shows the usual type of twinning. That is where you have two zygotes. That is the mother sloughed two ovum, not just one, and both were fertilized and both came down and were implanted in the uterus and they grew two fetuses, and they are called womb mates because they share the womb.

Well, we also can have twins, and the next chart shows identical twins and what happens with identical twins.

FIG. 4-19
Drawings showing how monozygotic (identical) twins develop from one zygote. They result from the division of blastomeres at various stages of cleavage (see Figs. 1-3 to 1-5). The separation may occur at the two-cell to morula stage, in which case two blastocysts develop and implant separately. Each embryo has its own placenta and chorionic sac, similar to that which occurs in dizygotic twinning (see Fig. 4-18). In these cases, it is not possible to determine from the membranes alone whether the twins are monozygotic (MZ) or dizygotic (DZ). In most cases, MZ twinning occurs at the early blastocyst stage. The inner cell mass, as shown, splits into two separate groups of embryonic cells. The two embryos that develop have separate amnions but a common chorionic sac and placenta (see also Fig. 4-20, *B*). Often, there is anastomosis of the placental vessels, but this is of no consequence because the flow of blood is similar in both directions. In 15% to 30% of monochorionic diamniotic MZ twins, there is a shunt of arterial blood from one twin through arteriovenous anastomoses into the venous circulation of the other twin. The donor twin is small, pale, and anemic, whereas the recipient twin is large and polycythemic. This condition is known as twin-transfusion syndrome (see Fig. 4-26).

This can occur apparently in at least two different stages in the development of the embryo. Here we have the zygote, which is the union of the egg and the sperm, and that then divides to two cells; and they have left out a lot of stages here because there are a lot of stages between the two cell and the inner mass cell stage.

These embryos can split at the two-cell stage or later on when they grow two inner cell masses. You can tell at what time they split by how they present themselves. If they are presented in two placentas, they split early and they go their separate ways. If they split later, they are generally presented at birth in a single placenta so the doctor knows the approximate time they split.

I recognized what was really happening here was in a sense you were taking half of the cells away from the original embryo, and both halves went on to produce a perfectly normal baby. So it seemed perfectly logical to me that you ought to be able to take a cell or two from an early embryo without hurting the embryo. There has been a lot of research since then.

By the way, the experts at NIH said, yes, that should be feasible. I mentioned this to the President at an event where we had just a few moments to talk about it, and he turned the pursuit of this over to Karl Rove who went to NIH and asked them about my suggestion, that you might be able to take cells from an early embryo, and he came back and called me and said they tell me they cannot do that.

I said either they did not understand the question or there is some confusion, because these are the same people that can take a single cell and take the nucleus out of that cell and put another one in it. That is what you do in cloning. If you can do that in a single cell, obviously you have the capability of taking a single cell out of a fairly large mass of cells.

So he went back a second time and asked them and they told him the same thing, and so the President came down a few days later with his executive order that all the stem cell lines we have produced by destroying embryos; and since he was opposed to taking one life with the hope that you might help another life, he could not support the destruction of any additional embryos, but that Federal money could be used in pursuing research and medical applications using what he was told was roughly 60 lines of stem cells that were in existence at that time.

[Time: 22:45]

Several years later in my office, just this year, as a matter of fact, talking with the people from NIH, they explained how this misunderstanding occurred. It is awfully easy to have misunderstandings when your backgrounds are very different, which is one of the problems we have in dialogues, of course. You can think that you are carrying on a dialogue when you are really carrying on simultaneous monologues, which was apparently sort of what happened in this discussion between Karl Rove and NIH. Because what they had really told him was that they did not know if they could make a stem cell line from such an early embryo, and that is true, and that is why I wanted animal experimentation to determine whether you could do that or not.

Our next chart shows some of this progression, and it shows what we are talking about and what we were talking about there. This is half of the reproductive tract of a mother. It shows an ovary, and there is one on each side, of course. Then it shows a funnel-like thing that sweeps over the ovum, it is called the infundibulum, and then the fallopian tube and down to the uterus. This shows just half of the tract. There is a mirror image of this over on the other side.

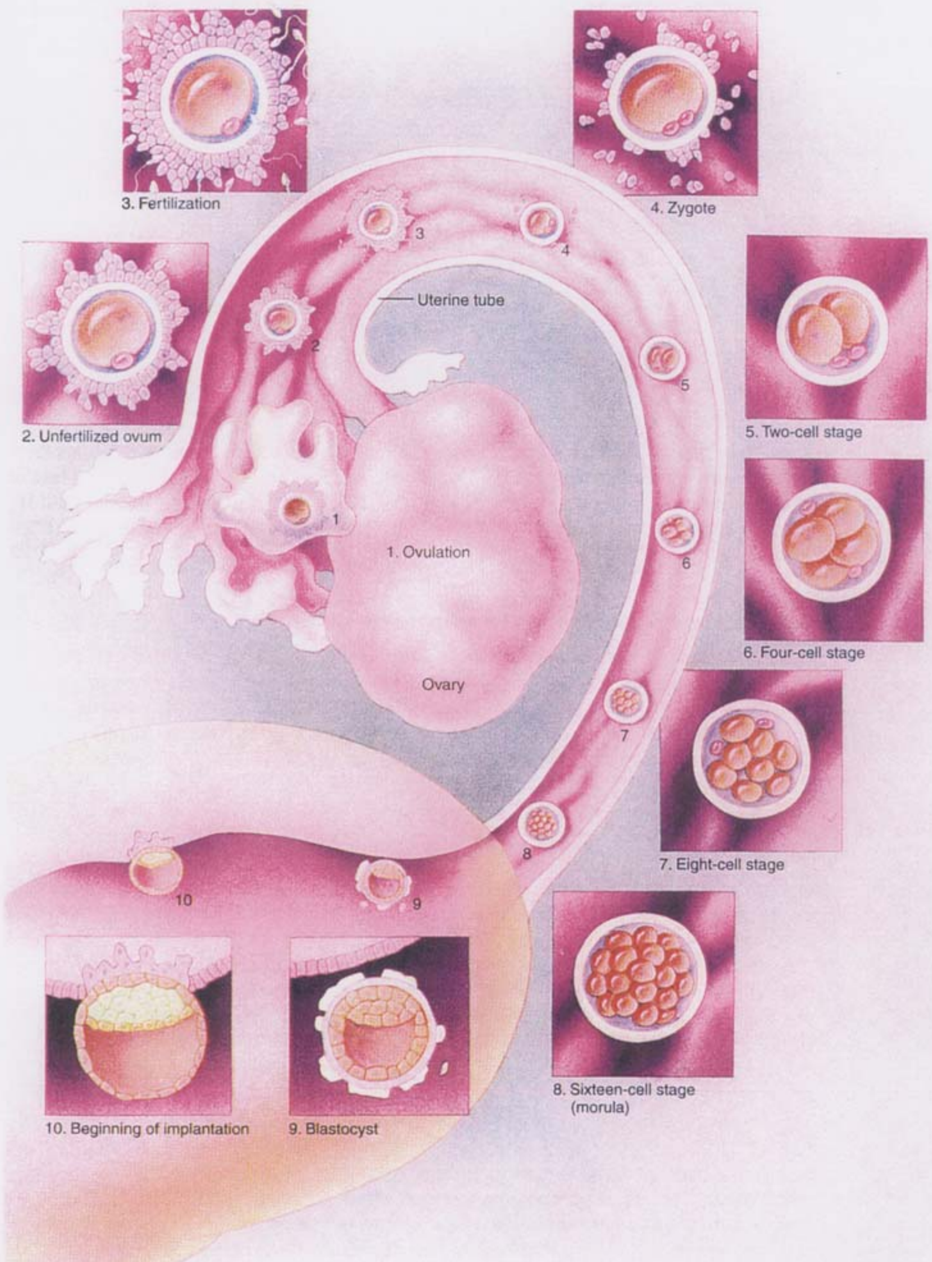

FIG. 1-4

Illustration of the first week of human development showing ovulation, fertilization, and cleavage of the zygote. Observe that the first two stages of development occur in the uterine tube. The morula enters the uterus on day 3 and the blastocyst forms on day 4, stage 3 of development (see Fig. 1-3). After floating in the uterus for about two days, the blastocyst begins to implant in the endometrium of the uterus.

By the way, there is an interesting thing that sometimes happens. These sperm are very energetic. They are released, of course, in the vagina of the mother, and they then make their way up into the uterus, through the cervix into the uterus, and then they swim all the way up the fallopian tube, and they can swim out through the end of the fallopian tube out into the body cavity. Sometimes the egg is not picked up by the cilia in the fallopian tube, and it also floats out into the body cavity, and the egg can be fertilized there. We call this an ectopic pregnancy and, of course, the baby cannot grow there, so that has to be removed.

The ovum starts down the fallopian tube and very high up in the fallopian tube, it is fertilized. Then it divides into two cells and four cells and eight cells. It is at the eight-cell stage in the laboratory. This same process of fertilization and growth occurs in the petri dish in the laboratory, and it is at the eight-cell stage in the laboratory that they ordinarily implant the embryos. This goes on, of course, to produce the inner cell mass that we saw in the earlier chart, which then differentiates into the germ layers. It is at these later stages that it actually implants in the mother's uterus.

The convention is ordinarily that implantation is done at the eight-cell stage. So my suggestion was that you could take a cell from the eight-cell stage, and it would not harm the embryo. As a matter of fact, if the embryo splits at this stage or at the two-cell stage or down here at the inner cell mass stage of the two inner cell masses, both groups of cells go on to produce a perfectly normal baby. So, obviously, there was the potential that you could take a cell from an early embryo without harming the embryo.

I have been carrying on this dialogue with the pro-life community and with the scientists at NIH now for these 4 years. During one of these discussions, the representative of the Catholic bishops, Mr. Doerflinger, made a suggestion. There are some things that you see in life that are just so obvious that you say, gee, why didn't I think of that. His contribution was just that kind of thing. He said, in addition to taking a cell out of that inner cell mass, and, by the way, this has now been done more than a thousand times around the world. We do not know how many more than a thousand times. But in the laboratory they want to know that this embryo they are going to implant in the mother does not have any genetic defects so that they are going to have a healthy baby.

So they take a cell out of the eight-cell stage and they do a pre-implantation genetic diagnosis on it and then they implant those remaining cells in the mother and more than a thousand times they have had a normal baby born.

Mr. Doerflinger's suggestion was, and in addition to doing that pre-implantation genetic diagnosis that you also establish a repair kit. That is kind of what you hope you are doing when you freeze umbilical cord blood. You hope that there are some stem-cell-like cells in there, that if there are future medical problems and stem cell research development has gone on to the point that you can make some meaningful applications that you could then be using tissues that would not be rejected like the tissues from an embryonic stem cell from another person.

But clearly if the repair kit was established from a cell taken from an early embryo, it would be exactly the genetic composition of the child, of the person, of the adult as they grew, and so any defect could then be very effectively treated with tissues that would not be rejected.

The President has a group of people, the President's Council on Bioethics, and because of the enormous expected potential from stem cell research, they have been looking at alternatives for embryonic stem cell research that might be ethically acceptable and they have just fairly recently issued a report, Alternative Sources of Human Pluripotent Stem Cells. It is called a white paper. In the body of that white paper they describe four different techniques.

The next chart shows a little paragraph from that, and I have highlighted a part of it.

24 ALTERNATIVE SOURCES OF HUMAN PLURIPOTENT STEM CELLS

II. Pluripotent Stem Cells via Blastomere Extraction from Living Embryos

Pluripotent stem cell lines could, in theory, be derived starting from small numbers of cells ("blastomeres") removed from *living* human embryos. Is there a stage of early human embryonic development at which cells, capable of developing in vitro into pluripotent stem cells, can be extracted without harming the embryo's prospects for developing into a live-born child?*

Blastomere extraction from living IVF embryos is currently performed to conduct what is called "preimplantation genetic diagnosis" (PGD). PGD is a procedure increasingly being used in conjunction with assisted reproductive technologies to test IVF embryos for genetic and chromosomal abnormalities prior to uterine transfer for beginning a pregnancy. PGD generally involves removal of a blastomere or two from living 6-8-cell embryos, and subsequent genetic tests on the removed blastomeres. Following the genetic screening, the desired embryos, from which one or two blastomeres have been removed, are then transferred to women to initiate pregnancy. Although estimates vary widely, one recent report suggested that more than 1,000 babies had been born

* At present, embryonic stem cells are typically derived by extracting cells from the inner cell mass of the embryo at the blastocyst (roughly 100-cell) stage; this entails the destruction of the trophectoderm (that is, the outer ring of cells in the spherical blastocyst structure, the precursor of the fetal contribution to the placenta) and the death of the embryo.

A WHITE PAPER OF THE PRESIDENT'S COUNCIL ON BIOETHICS 25

worldwide following PGD.[12] Thus, apparently normal children have been born following removal of one or two blastomeres from the 6-8-cell embryo. However, long-term studies to determine whether this procedure produces subtle or later-developing injury in children born following PGD have been recommended[13] and are sorely needed.

As indicated above, Dr. Nicolai Strelchenko and his colleagues have shown that embryonic stem cells can be derived from human embryos containing 8-24 cells (see reference 7). In their method, *all* the cells of the embryo are disaggregated and cultured on feeder cells (and the embryo is killed in the process). It may be some time before stem cell lines can be reliably derived from *single* cells extracted from early embryos, and in ways that do no harm to the embryo thus biopsied. But the initial success of the Verlinsky group's efforts at least raises the future possibility that pluripotent stem cells could be derived from single blastomeres removed from early human embryos without apparently harming them.*

A. *Is It Ethically Sound?*

1. *Harm to the embryo?*

With the Landry-Zucker proposal, the major ethical issue concerned the question of whether the embryos would in fact be truly dead. Here, the major ethical issue

* A similar idea was proposed by Representative Roscoe Bartlett of Maryland as far back as 2001.

It says it may be some time before stem cells can be reliably derived from single cells extracted from early embryos and in ways that do no harm to the embryo, thus biopsied. But the initial success of the Verlinsky's Group's efforts at least raises the future possibility that pluripotent stem cells could be derived from single blastomeres. A blastomere is simply a cell from the blastula. It merely means a cell removed from the early human embryos without apparently harming them.

Then there is a little asterisk. If you go to the bottom of the page you see, ``A similar idea was proposed by Representative **ROSCOE BARTLETT** of Maryland as far back as 2001.'' This is the proposal that I made to the President that was pursued by Karl Rove with the misunderstandings that we talked about a few minutes ago.

In the body of their paper, they talk about four different approaches. One of the approaches is to use embryos that obviously are not going to live because they are really bad and they are going to die. You could take cells from them like taking an organ from a person who is brain dead. I would have a little concern, Mr. Speaker, about how good a stem cell I was getting from an embryo that was dead.

Another suggestion is to manipulate the genes of the cells so that if they develop they will never produce a baby. It would be kind of a freak, I guess, and since it is not going to be a baby, then you could take cells from that. Again, I would have a little concern, was I really getting a normal cell when I was taking it from something that was genetically engineered so that it was not going to grow to be a baby?

In the text of their white paper, they do a very good job of talking about developing the repair kit and the fact that the cells could probably be taken without hurting the embryo. They look at all of the pluses and minuses of this.

But then it looks almost like, Mr. Speaker, that somebody else wrote the recommendations, because let me read from the recommendations here. The recommendations say, the second proposal, blastomere extraction from living embryos, we find this proposal to be ethically unacceptable in humans owing to the reasons given in the ethical analysis: We should not impose risk on living embryos destined to become children for the sake of getting stem cells for research.

I agree. That is not what they talked about in the text of their white paper. There they talked about pre-implantation genetic diagnosis. This clearly has to be for the benefit of the baby. The mother does not want to have a baby that is going to have a less than optimum opportunity for a good life with a genetic defect, and she has the opportunity to determine that and so she does it. And then they also talk about developing the repair kit.

So what we were proposing is that there would be cells made available, surplus cells from the repair kit, only after the parents had made three decisions which were in the interest of their baby. The first decision was to do in vitro fertilization. I know that there are those who do not believe that we ought to be doing in vitro fertilization. They kind of think that is like playing God. But there is an old axiom that I really subscribe to, Mr. Speaker, and that is that man's extremity is God's opportunity and God is not going to do for us what we can do for ourselves. And these parents have made the decision they want a baby and in vitro fertilization is the only way they are going to get one, so they have made the decision.

Then they have made the decision they really want a healthy baby, so they are going to do pre-implantation genetic diagnosis. And, by the way, they refreeze the embryo that was defective. It could be adopted. There are some families and, God bless them, that are really fulfilled by taking into their home handicapped babies, babies with defects, that they are going to be with them for a lifetime and these people feel fulfilled in taking these children into their homes, children who have HIV, crack cocaine babies and so forth and so these embryos could be adopted.

By the way, this is not genetic engineering. There have been some suggestions that this is an unacceptable technique. Just looking at what kind of genes are there, Mr. Speaker, that is not genetic engineering. That is not a very believable argument against this.

Then the parents have made a third choice, and that is to establish a repair kit for their baby. And only after the parents have made those three what I think are ethical choices, they want to have their own baby, they do not want their baby to have a genetic defect and they want their baby to have a repair kit and only after they have made those three decisions, then we would ask for some surplus cells from the repair kit to establish a new stem cell line.

There are two things that I want to refer to here. One is a letter from Dr. Battey, who is the spokesperson at NIH for stem cell research. He wrote me on May 23, fairly recently, a three-page letter in which he says, live births resulting from embryos which undergo pre-implantation genetic diagnosis and are subsequently implanted seem to suggest that this procedure does not harm the embryo. At least for a thousand times we have had a normal baby. They are not adults yet, and so the clock has to run for a while before we determine whether there is any defect.

I would be very surprised, Mr. Speaker, if there is a defect. Because you can take half the cells away from an early embryo to produce identical twins, and both halves produce what looks like perfectly normal people. So I would be surprised if there are any long-term effects from this.

Also, it is not known if the single cell removed from the eight-cell stage human embryo has the capacity to become an embryo if cultured in the appropriate environment.

Then I would like to turn, Mr. Speaker, to the Science section, Monday, June 6, just yesterday, Stem Cell Advances May Make Moral Issue Moot. A Dr. Lanza, and our office has spoken to Dr. Lanza, he is publishing a paper imminently. Some of the details could not be in this article because he was holding those for his paper.

In one approach pioneered by Robert Lanza and colleagues at Advanced Cell Technology in Worcester, Massachusetts, researchers plucked single cells from eight-cell embryos, embryos so young they do not have stem cells yet. Stem cells are ordinarily derived from inner cell mass. I do not understand saying that these are not the conventional stem cells but they certainly, I think, have the capacity to produce stem cells.

Fertility doctors have known for years that early embryos seem unfazed by the removal of any one of their eight virtually identical cells called blastomeres. In fact, it is common today to remove a single representative blastomere from a laboratory conceived embryo and test that cell for diseased genes before deciding whether to transfer that embryo into a woman's womb.

If this technique were applied to humans, and I skipped a couple of paragraphs where he talks about work with animals, if this technique were applied to humans, then a single cell taken from an eight-cell fertility clinic embryo could give rise to a self-replicating line of embryonic stem cells without compromising the donor embryo's odds of someday growing into a baby.

So the thing that Dr. Battey said had not yet been, and he was correct because this paper is yet to be published, I think it may be published today or tomorrow, but he has now in mice, and if it is doable in mice it is probably doable in higher animals, including humans, that they have developed lines from a single cell taken from an early blastomere.

I would just like to spend a few moments now talking about the bill which we have filed. It has a number of cosponsors, and I am very pleased that several doctors in the House have signed on to our bill.

[Time: 23:00]

Our bill really has nothing to do with working on humans because we think that we ought to do some animal experimentation before we start working with humans. So what our bill does is simply to make some money available for a several-year study, and we ought to go up to nonhuman primates. These are animals like chimpanzees and the great apes. To make sure that what has been done in mice and what has been done more than 1,000 times in these clinics, and what has been done, of course, is taking cells from an early embryo without apparently hurting the embryo, that we could develop these cells into a stem cell line. That has now been done, as was noted in the paper yesterday. This is the science section of The Washington Post. So the potential is there to do this. And all that our research does is to ask for animal experimentation so that we can check and double-check and make really sure that this is a safe procedure for humans.

I would like to put up the last chart that we are going to refer to now. This is a little bit like one that we looked at previously. This shows again half of the reproductive tract of the female; and, of course, what we are talking about are procedures that are done in the laboratory. But they are mimicking what happens in the body. By the way, when the little baby girl is born, she has in her ovary all of the ova that will ever be there, and they mature generally during her reproductive life, which may span 30, 40 years. They generally mature from one side or the other one a month. But they are all in there. And this shows the development of these ovum. And finally they grow and there is like a little blister on the side of the ovary, and then it breaks and the ovum is free.

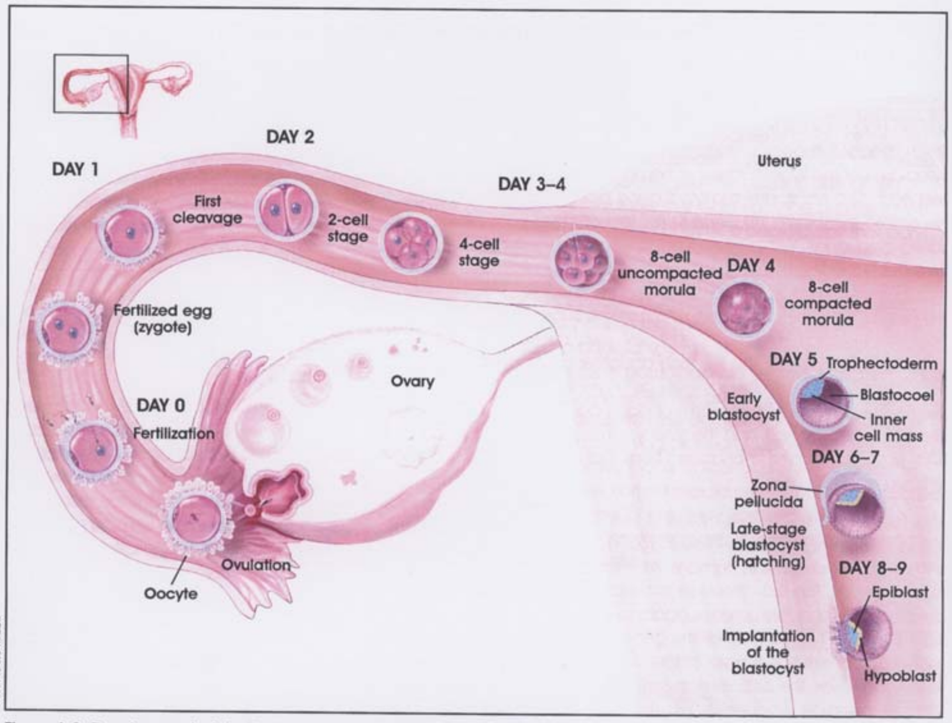

Figure A.2. Development of the Preimplantation Blastocyst in Humans.

small, round cells of the inner cell mass, and the fluid-filled blastocoel [19, 23].

By E4.0 in mice, and between 5 to 7 days post-fertilization in humans, the blastocyst reaches the uterus. It has not yet implanted into the uterine wall and is therefore still a pre-implantation embryo. When it arrives in the uterus, the blastocyst "hatches" out of the zona pellucida, the structure that originally surrounded the oocyte and that also prevented the implantation of the blastocyst into the wall of the oviduct [19]. (An embryo that does implant in the oviduct results in a tubal pregnancy, which can result in severe hemorrhaging.)

The nutritional requirements of the embryo change markedly during the time from zygote formation to the compaction of the morula, to the development of the blastocyst. Also, the physiology and biochemistry of the cells change as they increase in number and begin to differentiate. For example, the primary sources of energy for the cleavage-stage embryo are pyruvate, lactate, and amino acids—simple molecules that play important roles in various metabolic pathways. But after compaction of the morula, glucose is taken up by the embryo and used as a primary source of energy [15]. Indeed, mammalian blastocysts may have a unique transporter molecule, GLUT8, that ferries glucose into the blastocyst. GLUT8 appears in the blastocyst at the same time as the receptor for insulin-like growth factor–1 (IGF-1). Thus, the blastocyst, which requires a great deal of energy at this stage of development, is equipped to respond to insulin by taking up glucose [7].

These and other observations about the preimplantation blastocyst have led to recommendations

In the laboratory, of course, these have been washed out of the reproductive tract of the female, and they are now put in petri dishes and exposed to sperm. In the body, the sperm is deposited in the vagina, makes its way through the cervix, up through the uterus, and swims clear up through the Fallopian tube. In a laboratory, of course, they simply with a pipette put the sperm in the petri dish with the ovum. And there will be many sperm. There are millions of sperm. And really quite a miraculous and very rapid transformation takes place. As soon as one sperm enters the egg, the egg then sets up a defense so that no more sperm can enter because if another sperm were able to make its way in and they had three sets of chromosomes instead of two, that would be fatal.

By the way, in flowers that is not fatal. That is called polyploidi, and that is how we get bigger flowers and better smell and so forth. But plants react very differently to extra chromosomes than humans do. Tisomy-21 produces mongoloid babies. That is just having one extra of one chromosome. So we do not react well to extra chromosomes; and so the ovum, after one sperm has entered, it sets up this defense so that no more sperm can enter.

The same thing happens in the laboratory. And then it divides, and the doctor watches that division. And down at the eight-cell stage, they take a cell out and do pre-implantation genetic diagnosis; and as recent research has demonstrated, the paper that is going to be published very shortly by Dr. Lanza, they have done this in mice, but if it is possible there, it ought to be possible in higher animals, and our research would determine that. They have produced stem cell lines from a single cell taken. What this means is, Mr. Speaker, that we now have been able to produce, we will be able to produce, embryonic stem cell lines without harming an embryo.

I have heard people say that they are just unalterably opposed to embryonic stem cell research. I hope that is not what they mean. I hope what they mean is that they are unalterably opposed to embryonic stem cell research if it means killing an embryo. I am unalterably opposed to embryonic stem cell research if it means taking one life with the hope that we will be able to help another life. But with these recent advances in medicine and research in the laboratory, there is the real hope that we can take cells from an early embryo to benefit the embryo.

And I would like to say again the reasons that the parents are taking cells from this early embryo, the fundamental reason they are taking the cell is to do a pre-implantation genetic diagnosis. And the President's Council on Bioethics mentions the possibility of creating a repair kit, which certainly would benefit the baby. So the parent has now done three things which they think are ethical. I think that they are ethical, and there ought to be surplus cells from the repair kit, and it is those surplus cells that would be made available for additional stem cell lines.

But I want to reiterate again that the bill which we have just looks at animal experimentation. Although human research, human developments, human applications have gone beyond some of the exploration that we have done with animals, we still think that it is prudent to work with animals where we can determine with more cases and more intense experimental observation to make sure that there are no untoward effects of doing this.

I hope that this research can bring the two sides together. We had a couple of weeks ago a very heated debate. The emotions on both sides were rather obvious: those who wanted to take some of these more than 400,000 frozen embryos that they said were going to be discarded anyhow to get some good from them, and they were so convinced of this in California that they voted for $3 billion to proceed with this. The argument on the other side, which position I take, is that morally I have big problems with taking one life, and this little embryo could become under the right circumstances a baby. More than 100 times it has. From these frozen 400,000, there are about 100 or so, we call Snowflake babies, because this is a program to offer these embryos for adoption, and more than 100 times they have been adopted, and the President had some of those babies at the White House a couple of weeks ago when we were having that debate, and they came to the Hill also when we were having that debate here on the floor.

With the ability to take cells from an early embryo not to establish a stem cell line, that is not why the parents took it. They took the cell to do a pre-implantation genetic diagnosis. They then would like to establish a repair kit. We know they would like to do that because they are more and more freezing umbilical cord blood, which, as the one doctor I read from said, is a poor second choice to an embryonic stem cell line, but it is better than nothing. So we know that parents would like to do that. And it is only after that if the animal experimentation supported by our bill shows that this is efficacious and will not harm the baby, only after that would stem cell lines be derived from surplus cells from repair kits that the parents had decided to establish for the benefit of their baby.

I think, Mr. Speaker, that this ought to remove all of the ethical objections. But there is just one more, and I just want to spend a moment talking about that, and this is a good chart to talk about it from. Since these cells at the eight-cell stage are quite undifferentiated, which means they have not really decided what they are going to be, it is possible that they might take that one cell and establish another embryo. The President's Council on Bioethics thinks that is very unlikely. But what I would like to see them pursue is the development of stem cell lines and the pre-implantation genetic diagnosis from the inner cell mass stage.

Now, that is the stage at which embryonic stem cells are ordinarily taken from when the embryo is destroyed. That is before the embryo is implanted in the normal process. Here is the inner cell mass, and here is where it is implanted a couple of days later, 2 or 3 days later, in the uterus.

[Time: 23:10]

Ordinarily, and I am not sure why they use the eight cell stage in the clinical laboratories, but I would like to see cells taken from the inner cell mass. There is no ethical question involved there because these cells in the inner cell mass cannot produce a baby because they have already lost their ability to produce decidua. The decidua is the amnion and chorion which is commonly known as the placenta, and they have lost the ability to do that, so they cannot produce a baby, but they can produce all of the tissues of a person, because these are what produce, back to our first chart that shows the inner cell mass differentiating into these three germ layers.

So the last possible ethical objection to deriving stem cells from pre-implantation genetic diagnosis and the development of a repair kit would be gone if we could take the cell from the inner cell mass, because the inner cell mass, those cells could not possibly produce a baby, because they are sufficiently differentiated that they cannot produce the decidium.

I have used this term ``differentiation'' a number of times, and what we try to do with adult stem cells, because they are already differentiated, we try to de-differentiate them. We try to confuse them with biological cues, with chemicals, with exposing them to other cells and the products from other cells so that they can kind of forget their development and they now go back to a prior less-differentiated state where they could produce more variety of cells. But you avoid those problems with the embryonic stem cell, because it has the capability to produce any and every cell in the body.

Mr. Speaker, I believe that with these recent medical advances, with the knowledge that we have, that it is perfectly feasible to ethically develop embryonic stem cell lines from embryos which should have, in the view of many of the experts, and clearly in the view of most Americans if you poll them, should have more potential than adult stem cells. Only research will tell that, and only time will tell whether or not that is true.

But with the hope that these large numbers of diseases so devastating to our people could be affected or maybe cured with embryonic stem cells, we really must pursue this, and now we have the opportunity to do that without offending those who have a problem with taking one life so that we might help another life.

I think, Mr. Speaker, that we now are on the cusp of advances that will bring these two sides together. We have enough things to be concerned about and to discuss in our country, we do not need to be discussing this, and I think the two sides with these present advances can come together. I hope that we will have an early vote on our bill and it will reach the President's desk so that he has a bill that he can sign that will promote embryonic stem cell research.